



What Do Exposure and Dosimetry Studies Tell Us about the Dose to the Susceptible Populations?

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research
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Science Question

The respiratory dose of inhaled particles depends on morphological and physiological conditions in the lungs of individual subjects. Thus, variations in the dose of particles delivered to various locations in the lung may be expected in susceptible populations, compared to the dose delivered to healthy populations. In addition, the disease state of certain susceptible subgroups may result in altered behavior (e.g. more time spent indoors), which could also affect the dose of particles they receive.

The key questions are then:

- What are the exposure-dose relationships for susceptible populations compared with those for normal subjects?
- What is the relationship between ambient PM and personal exposure to PM in potentially susceptible subpopulations?
- To what extent does enhanced respiratory dose play a role in determining susceptibility?
- If a higher dose is a crucial factor for susceptibility, are there any other subject groups that are susceptible but not yet identified?

Research Goals

- Obtain personal exposure measurements for susceptible populations under realistic living environments.
- Define exposure-dose relationships in susceptible populations.
- Determine deposition distribution within the respiratory tract and identify local regions of dose enhancement.
- Assess the factors causing an excessive dose enhancement in the lung, particularly in patients with obstructive airway disease.
- Assess the microdose relevant to tissue burden and subsequent reactions.

Methods/Approach

Exposure Assessment

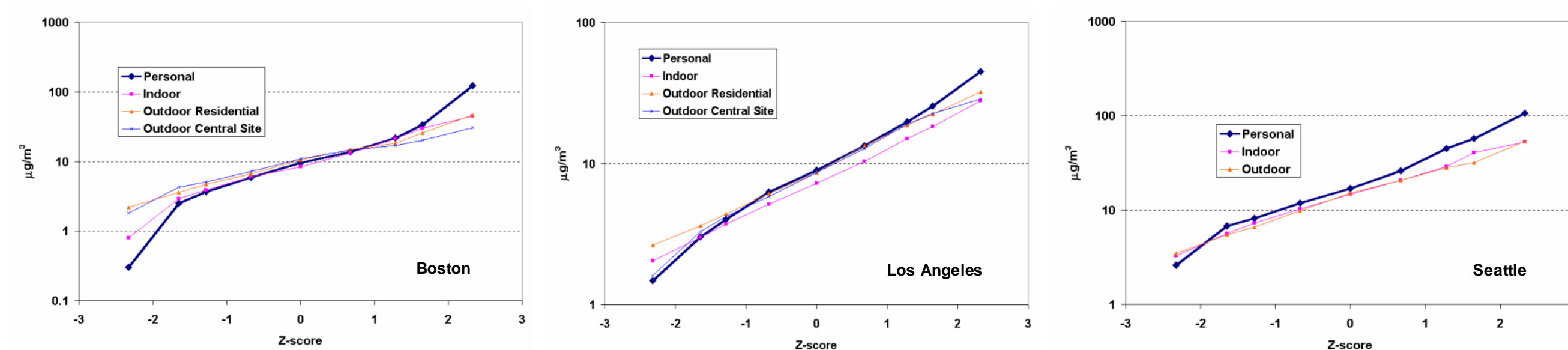
- Personal samples (PEM_{2.5}) were obtained and compared with indoor, outdoor and fixed central station samples in five different cities. The impact of seasonality was also investigated.
- Personal samples were obtained from four different subject groups including COPD, CHD, children and healthy elderly subjects and compared to see if personal microenvironment may contribute to the susceptibility.

Respiratory Dose Measurement

- Total and regional lung deposition values were measured in normal and susceptible populations including the elderly, COPD and asthmatics under controlled and spontaneous breathing conditions.
- Lung deposition was measured with different size particles (ultrafine, fine and coarse) and different breathing patterns.
- Respiratory deposition was analyzed in correlation with measures of obstructive airway disease.

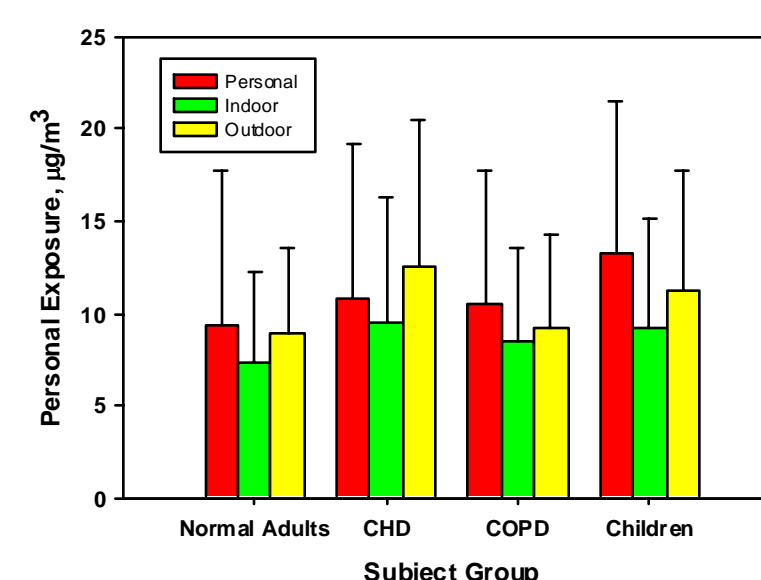
Exposure Study Results

Comparison of Personal Exposure (PM_{2.5}) with Indoor, Outdoor and Fixed Station Measurements in 3 Cities

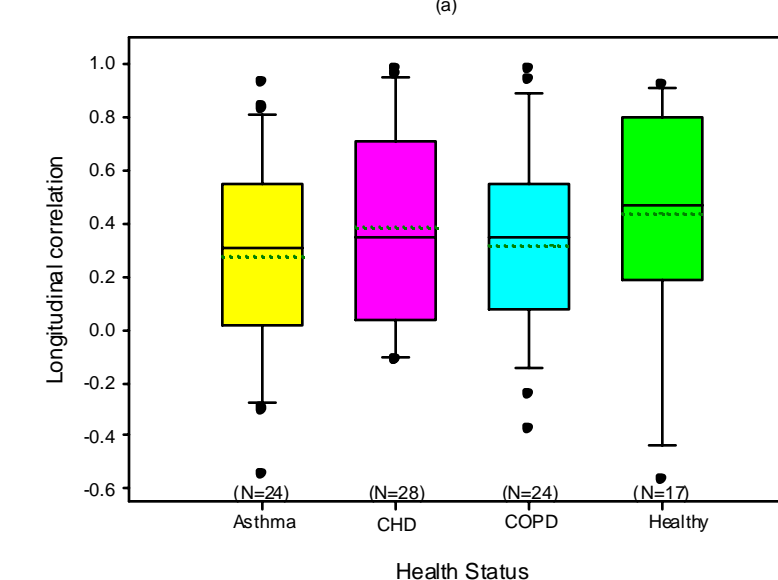


Personal exposure (PM_{2.5}) in comparison with indoor, outdoor and central station measurements in three geographically different cities. The correlations between mass concentrations measured at outdoor central sites and at the personal level were often on the order of 0.40 or lower. However, the levels of personal exposure are in phase with changes in indoor and outdoor concentrations.

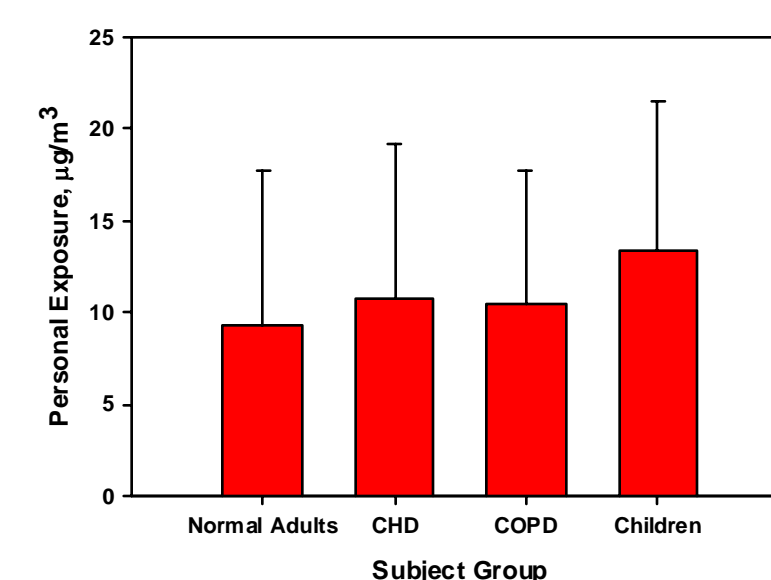
Personal Exposure Measurements (PM_{2.5}) in Susceptible Subpopulations



Relationships of personal PM_{2.5} with indoor and outdoor measurements are consistent among four different subject groups.



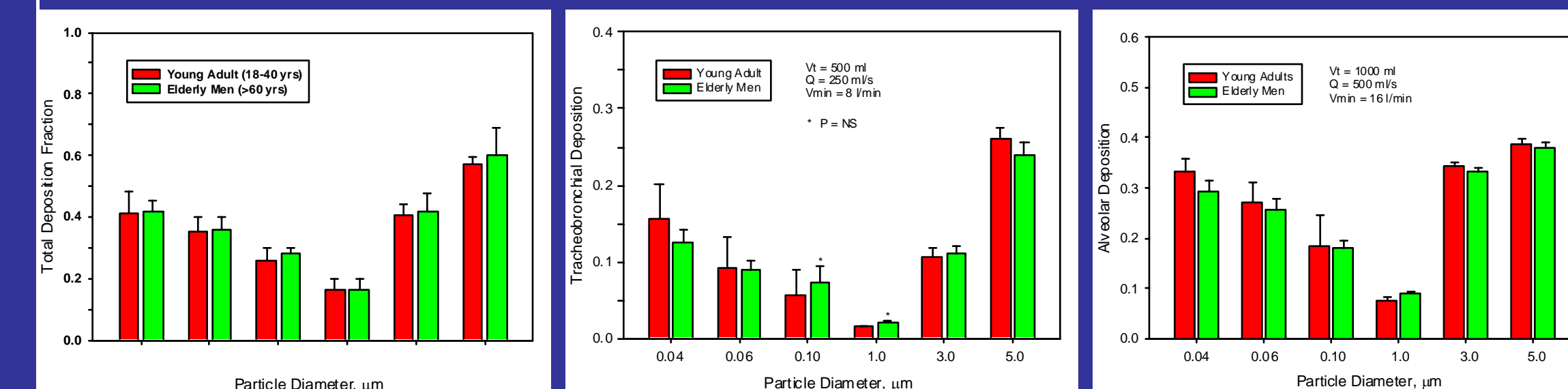
Longitudinal correlation between personal PM_{2.5} and central measurements are comparable among four different subject groups.



Personal PM_{2.5} measurements are similar for the healthy and sick cohorts. Some variations seen in the graph are probably the result of time activity pattern differences among the subject groups, especially the children.

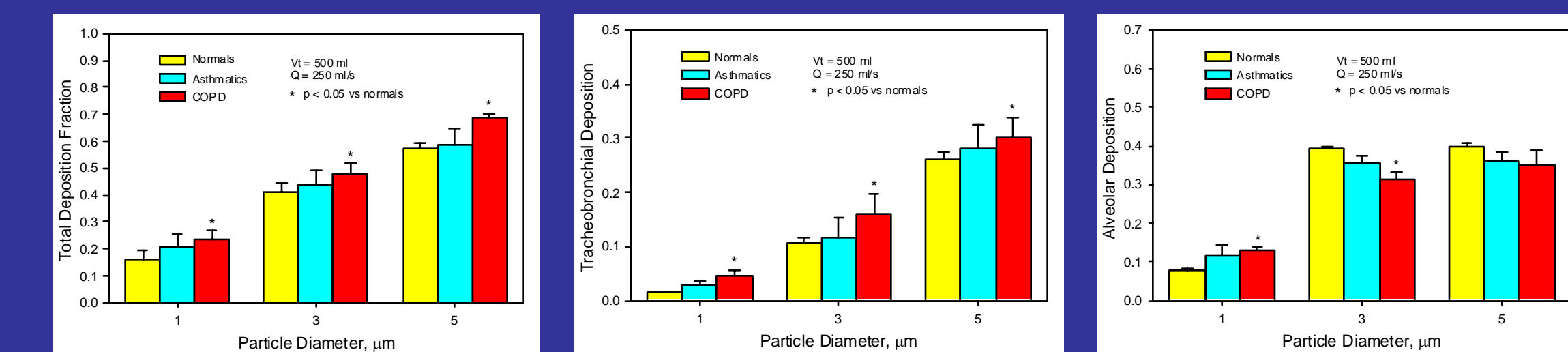
Dosimetry Study Results

Total and Regional Deposition in the Lungs of Healthy Elderly Subjects



Total as well as regional (tracheobronchial and alveolar) lung deposition is essentially the same for both elderly and young adults during normal controlled breathing in a wide range of particle sizes (ultrafine, fine and coarse particles).

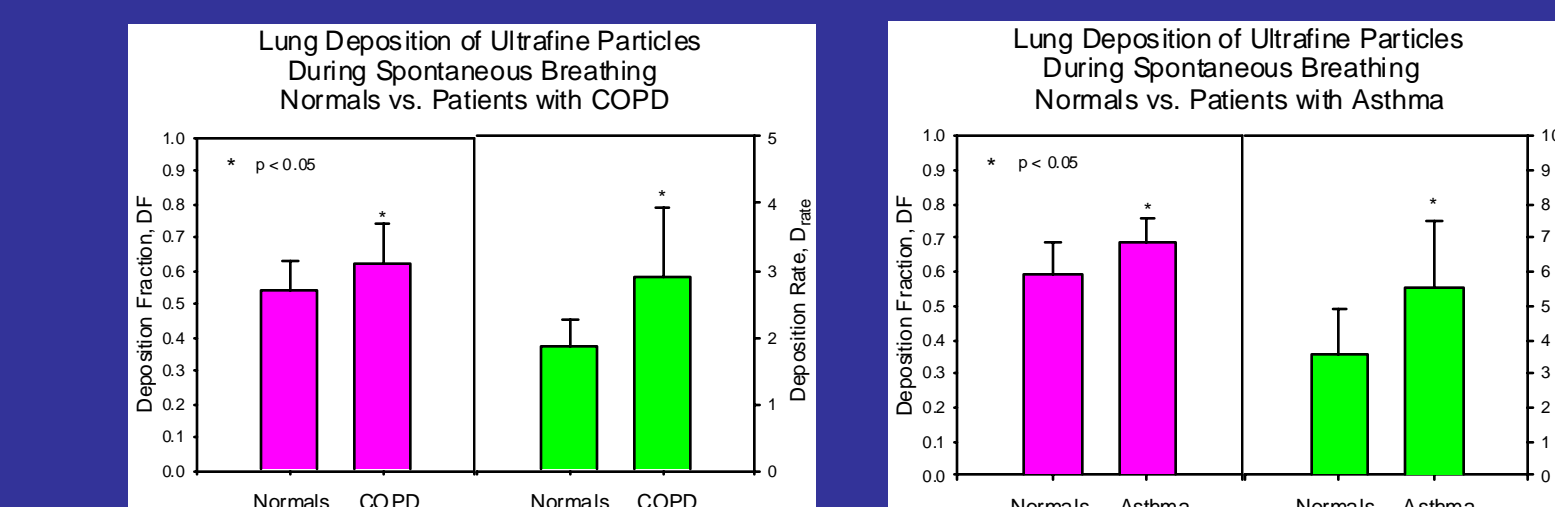
Total and Regional Deposition in the Lungs of Asthmatic and COPD Patients



Total lung and tracheobronchial deposition increases in patients with obstructive airway disease such as asthma and COPD.

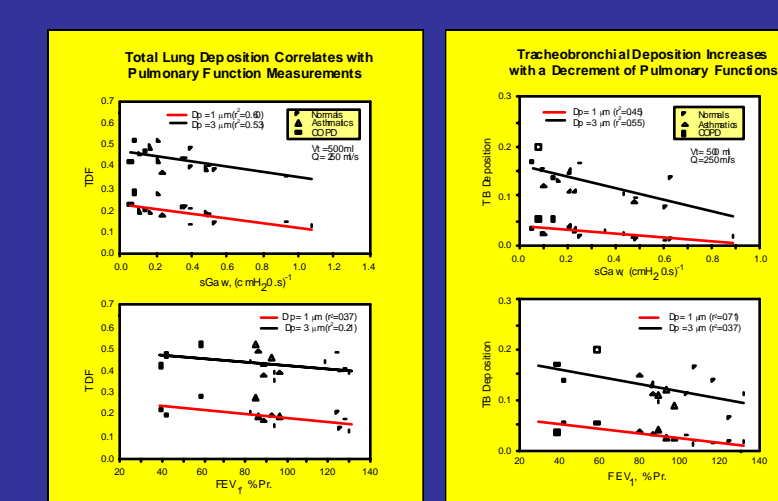
Alveolar deposition, however, tends to decrease in the patients for coarse particles.

Total Lung Deposition of Ultrafine Particles in patients with Asthma and COPD



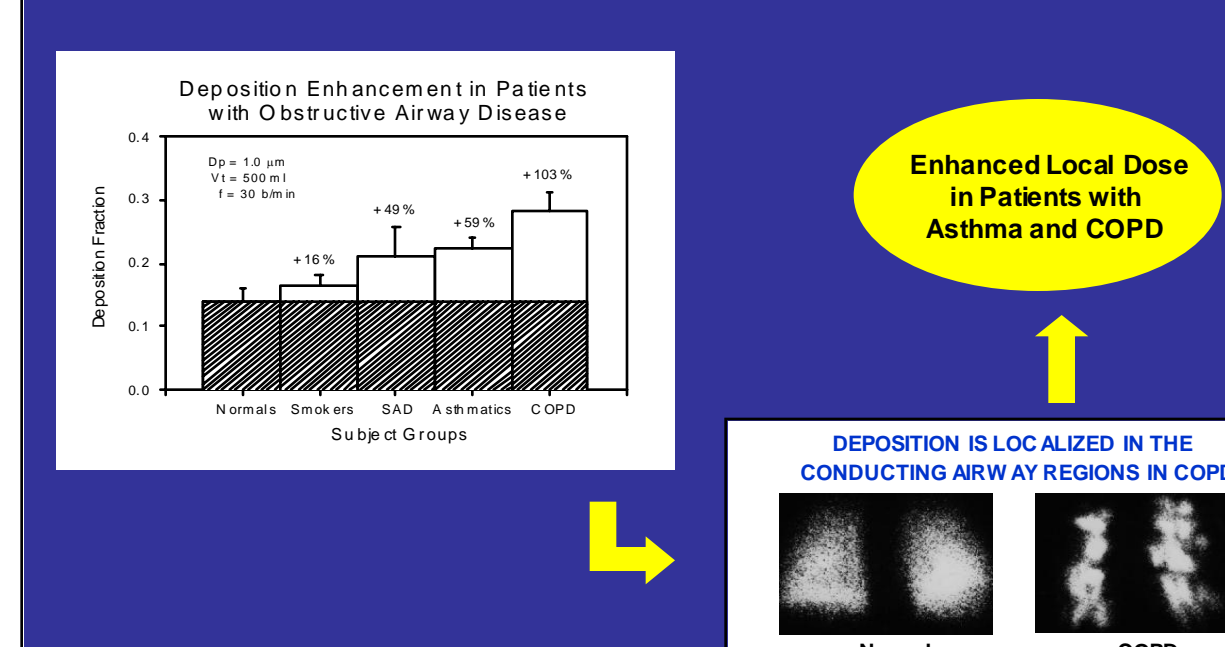
- Total lung deposition of ultrafine particles increases per breath in patients with asthma and COPD during spontaneous breathing.
- Deposition rate increases to a greater extent because of greater minute ventilation of people with asthma and COPD.

Lung Deposition vs. Pulmonary Function



Both total and tracheobronchial deposition correlate well with measures of airways obstruction: an increase in deposition with increasing degree of obstruction.

Marked Enhancement of Local Dose is the Hallmark of COPD Lungs and a Potential Risk Factor



Summary of Results

- Personal exposure levels are comparable among different subject groups including the elderly and cardiopulmonary patients. Thus, respiratory dose may be determined primarily by internal factors.
- Lung deposition is comparable between young adults and healthy elderly subjects under the same exposure conditions indicating that the age itself does not alter exposure-dose relationships in adults.
- Lung deposition is increased in patients with obstructive airway disease such as asthma and COPD. Deposition enhancement is remarkable, particularly at local sites.
- Marked enhancement of local dose may be a crucial factor for local tissue response and eventual adverse health outcomes.

Future Directions

- Determine if differences exist in particle deposition in other potentially susceptible populations (e.g. obese).
- Better understanding of the clearance and fate of particles.
- Establish reliable exposure-dose relationships for susceptible populations.
- Development of mathematical models for estimating dose under chronic exposure conditions and for extrapolation from animal models of disease to humans.
- Define the factors that affect personal exposures to PM of ambient origin.
- Determine if personal exposure and dosimetry parameters are the same for PM derived from different sources.

Impact and Outcomes

- Because particles are deposited with greater efficiency and in concentrated local "hot spots" in susceptible populations, the internal dose delivered to these populations is higher than for healthy individuals. The EPA may need to take these differences into account when considering the next revision of the PM standard.
- Enhanced local rather than the total lung dose may be a better dose metric for estimating the risk of PM exposure in susceptible populations.
- The time activity patterns rather than disease state would appear to be a more important variable for personal exposure to PM of outdoor origin in susceptible populations.

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Health and Exposure